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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/525,797	03/15/2000	Athanasius A Anagnostou	5218-39B	9917

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MYERS BIGEL SIBLEY & SAJOVEC
PO BOX 37428
RALEIGH, NC 27627

EXAMINER	
UNGAR, SUSAN NMN	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 01/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/525,797	ANAGNOSTOU ET AL.	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *02 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *12,15,19-21,23-26 and 31-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *12,15,19-21,23-26 and 31-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *November 2, 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. The Amendment and Declaration filed November 2, 2005 in response to the Office Action of June 30, 2005 is acknowledged and has been entered. Previously pending claims 12, 15, 19-21, 23-26, 31-33 have been amended, Claims 34-35 have been added. Claims 13-14 have been canceled. Claims 12, 15, 19-21, 23-26, 31-35 are currently being examined.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The following rejections are being maintained:

Claim Rejections - 35 USC 103

4. Claims 12, 15, 19-21, 23-26, 31-33 remain rejected under 35 USC 103 and newly added claims 34-35 are rejected under 35 USC 103 for the reasons previously set forth in the paper mailed June 30, 2005, Section 4, pages 2-3.

Applicant argues that none of the cited references teach or suggest the currently amended independent claims 12 and 21 because the Sigounas Declaration teaches that cancer patients typically receive EPO only after being diagnosed with anemia, thus references directed to administration of EPO to anemic cancer patients do not teach or suggest providing EPO prior to administration of a chemotherapeutic agent wherein said EPO is administered in an amount effective to enhance suppression of endothelial growth associated with administration of said chemotherapeutic agents as recited in Claim 1 or when administered in an amount of from about 750 Units per kilogram to about 2000 Units per kilogram as recited in claim 21. The argument has been considered but has not been found persuasive because neither the specification nor the claims are drawn to the administration of EPO at any particular time during the chemotherapy treatment. As previously set forth, "since the reference teaches that the patients were

receiving concomitant chemotherapy regiments, the erythropoietin was clearly being administered concurrently, prior to and after cisplatin administration, thus the prior art reference meets the limitations of the claims. Further, as drawn to the dosage claimed, again as previously set forth, "since the specification does not teach a specific time for the administration of the erythropoietin and the claims are not limited to a specific time, the instant reference meets the dosage limitation of the claims (please see page 5 of the action mailed December 28, 2004). In addition, as drawn to the administration of about 750 Units per kilogram to about 2000 Units per kilogram it is noted that the Sigounas Declaration is not commensurate in scope with the claimed invention since, in the animal model presented, only 60 Units per kilogram were administered prior to administration of the chemotherapeutic agent (see p. 4 of the Declaration).

Applicant argues that the *in vivo* data presented in the Sigounas Declaration demonstrates that EPO followed by cisplatin potentiates the action of cisplatin on reduction of tumor mass in an animal model. Given this information in combination with the experimental data presented in the specification, Applicants respectfully submit that the method of the cited references do not comprise the same method steps recited in the pending claims and that the presently recited methods are not anticipated because the method discussed in the cited references would not inherently lead to enhanced suppression of endothelial growth associated with administration of cisplatin. Further, the Sigounas Declaration argues that prior to 1996 it was not standard practice to administer EPO to anemic cancer patients prior to receiving treatment with a chemotherapeutic agent, instead anemic cancer patients who received EPO were administered EPO only after undergoing chemotherapy and after being diagnosed with anemia. The Declaration

further argues that solid tumors are not typically associated with anemia at the time of cancer diagnosis and/or chemotherapy.

The argument has been considered but has not been found persuasive because although it appears that Dr. Sigounas is correct and EPO is apparently not typically administered prior to the beginning of treatment for cancer with chemotherapy, the claims are not drawn to administration of EPO prior to the beginning of/first treatment for cancer with chemotherapy. For the reasons set forth previously and above, the reference(s) meets the limitations of the claims. Further, contrary to Applicant's arguments, the prior art reference(s) teaches the claimed method steps as clearly elucidated previously and above. Nothing in the claims requires that the EPO be administered prior to the first chemotherapy treatment.

Applicant further argues that one would not have a reasonable expectation of success of treating patients with hemangioblastoma, ductal carcinoma of the breast or squamous cell carcinoma of the larynx using the protocol described by Bukowski et al and reiterates arguments previously set forth in the response dated March 28, 2005. The arguments have been considered previously but have not been found persuasive for the reasons of record.

Applicant argues that the other cited references do not supply the missing recitations or provide the motivation to administer EPO in the manner recited in the pending claims. The argument has been considered but has not been found persuasive because it does not appear that the 103 rejection is drawn to Bokkel et al or JP 02096535.

Applicant's arguments have not been found persuasive and the rejection is maintained.

Claim Rejections - 35 USC 102

5. Claims 12, 15, 19-21, 23-26, 31-33 remain rejected under 35 USC 102 and newly added claims 34-35 are rejected under 35 USC 102 for the reasons previously set forth in the paper mailed June 30, 2005, Section 5, pages 3-7.

Applicant puts response to rejections under 35 USC 102 and 103 under a single heading. The arguments set forth above have been considered for the rejection under 35 USC 102 and for the reasons set forth above, have not been found persuasive.

Applicant's arguments have not been found persuasive and the rejection is maintained.

New Grounds of Rejection

Claim Rejections - 35 USC 112

6. If Applicant were able to overcome the rejections set forth above, Claims 12, 19-21, 23-26, 31-35 would still be rejected under 35 USC 112, first paragraph because the specification, while being enabling for the claimed method wherein the claimed chemotherapeutic agent is cisplatin, does not reasonably provide enablement for the claimed method with administration of a chemotherapeutic agent. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The specification teaches that administration of increases doses of EPO enhance the endothelial growth-suppression caused by chemotherapeutic agents (para bridging pages 4-5). Endothelial-inhibiting amounts of EPO refer to those dosages which enhance or increase the suppression of endothelial growth/that decrease the numbers of viable endothelial cells following exposure to the chemotherapeutic agent. The most effective inhibiting amounts of EPO may vary

depending upon the time of administration and the etiology of endothelial damage (p. 6, lines 20-34). The specification further teaches that the term chemotherapeutic agent refers to cytotoxic antineoplastic agents, that is chemical agents which preferentially kill neoplastic cells or disrupt the cell cycle of rapidly proliferating cells (p. 9, lines 17-21). The present inventors have found that when EPO is administered (simultaneous with, before or after chemotherapeutic administration), the administration of the EPO enhances the endothelial growth inhibition seen with chemotherapeutic agents (p. 12, lines 10-15). Applicant exemplifies the inhibition of endothelial growth *in vitro* in cell culture assays with cisplatin in combination with EPO (see examples).

One cannot extrapolate the teaching of the specification to the scope of the claims because Applicant has clearly shown that the findings drawn to potentiation of CIS effects with EPO cannot be extrapolated to cancer chemotherapeutics other than CIS. In particular, the Sigounas Declaration discloses experiments drawn to determining the effects of EPO on potentiation of chemotherapeutic drugs, CIS, DDP (a form of cisplatin), MITO and CTX. Surprisingly, the only results reported or shown were results drawn to CIS and DDP, a form of cisplatin. Applicant explains the lack of data shown, at least in terms of MITO by stating on page 7 of the response that "Sequential administration of EPO and MITO showed a reduction in tumor mass compared to the reduction observed with MITO alone, however, this difference was not statistically significant (data not shown)." Given the lack of significant tumor mass reduction, it would appear that EPO does not potentiate the effects of MITO alone. Given the statements drawn to EPO/MITO, given that no data is presented for EPO and CTX, it is reasonable to assume that if any reduction in tumor mass was found with sequential administration of EPO and CTX, that it

also was not significant and that EPO does not potentiate the effects of CTX alone. Thus, it is clear that the finding that EPO potentiates the effects of CIS is a surprising event. Given the information in the Declaration and in the instant response, it appears that it cannot be predicted if any chemotherapeutic activity, other than CIS, can be potentiated by the prior administration of EPO or how to use the claimed invention if it does not potentiate the effects of the chemotherapeutic. Applicant is reminded that MPEP 2164.03 teaches that "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature ot the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to explicitly stated in the specification. In constrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling."

Given the teachings of the Declaration and the instant response, given the lack of adequate disclosure in the specification drawn to the broadly claimed chemotherapeutic, and in view of the surprising and complex nature of the claimed invention, and little is known in the art about the claimed invention, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

7. Claims 23-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 23-24 recite the limitation "said cisplatin". There is insufficient antecedent basis for this limitation in the claim 21 from which they depend.

8. No claims allowed.

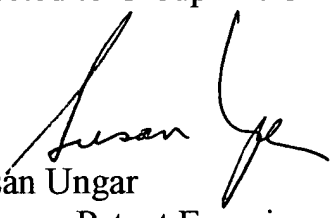
9. Applicant's amendment necessitated the new grounds of rejection. Thus, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at 571-272-0787. The fax phone number for this Art Unit is (571) 273-8300.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.



Susán Ungar
Primary Patent Examiner
January 18, 2006